REMARKS

Status of the Claims

Claims 1, 5, 6, 21, 22 and 25 to 27 are pending as shown above.

35 U.S.C. § 112, 1st paragraph, written description

Claims 1, 3-9, 21-22 and 25-27 were again rejected under 35 U.S.C. § 112, 1st paragraph as allegedly not adequately described by the as-filed specification. (Final Office Action, pages 2-6). In particular, it was again alleged that the claims encompass "limitless combinations" that have not been shown to work as biodetectors and that only the exemplified biodetectors are actually described. *Id.* It was also alleged that the specification teaches that one must empirically determine which combination of elements function as intended. (Final Office Action, page 3, citing pages 26-28 of the specification).

In response, Applicants again note that the rejection is legally untenable because the Examiner has improperly based a written description rejection on the grounds that embodiments must be "empirically determined." As noted by the Examiner, the written description requirement of Section 112 is separate from the enablement requirement. The written description requirement does not necessitate that Applicants list all possible embodiments (including embodiments that can be empirically determined). Rather, the relevant inquiry is whether the as-filed specification, in light of the state of the art, shows that Applicants were in possession of the claimed subject matter at the time of filing.

For the reasons of record, it is clear that, in view of the state of the art regarding fusion proteins involved in cascades and the as-filed specification's clear disclosure in this regard, Applicants have shown possession of the claimed subject matter.

In the instant case, the pending claims require a transmembrane fusion protein comprising an antibody portion that acts as an extracellular ligand-binding component and an intracellular phosphorylase or phosphatase domain. Binding of the ligand to the antibody domain activates the intracellular phosphorylase or phosphatase domain. In turn, the phosphorylase or phosphatase activates a transducer protein which then acts on a promoter operably linked to a light-generating marker gene. Thus, the claims do not encompass "limitless

combinations" – the transmembrane fusion protein must include an antibody (in the extracellular portion) and an intracellular phosphorylase or phosphatase activated by binding to the antibody portion. Only transducer molecules activated by phosphorylation or dephosphorylation are encompassed by the claims.

Indeed, the specification clearly shows that Applicants were in possession of the claimed combinations of the specifically claimed biodetectors (page 11, lines 30-31; page 12, lines 4-9; page 14, lines 21-29; emphasis added)

> Once bound to a ligand, an enzymatic cascade is activated that serves to transmit the signal.
>
> Furthermore, as the ligand-specific domain of the signal converting element of the biodetector system may be exchanged like a cassette, an unlimited number of biodetectors can be generated to recognize any desired or selected substance. Thus, the biodetectors of the present invention provide a flexible, generic system that can be adapted to recognize any selected substance, out of a wide variety of choices.
>
> The signal converting element is composed of an "extracellular" portion selectively binding a specific substance and an "intracellular" portion capable of activating the transducer. Typically, the signal converting element will be a transmembrane fusion protein composed of an extracellular ligand-binding portion, *e.g.*, an antibody and an intracellular enzymatic portion, which is activated upon binding of the extracellular portion to a selected target. Accordingly, the signal converting element is designed to convert the recognizing and binding of a specific substance, *i.e.*, ligand into an intracellular signal, resulting in the activation of the transducer component, which in turn activates a promoter that drives the expression of the reporter protein.

Example 2 also presents a myriad of references demonstrating that, at the time of filing, the skilled artisan was also well aware that transmembrane antibody-phosphatase fusion proteins were known to induce expression of specific genes.

Applicants also strongly object to the assertion that, as in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), the genus encompassed by the claims is not adequately described. For the following reasons, the Office cannot rely on *Eli Lilly* to support its written description rejection in the pending case.

The fact-pattern in *Eli Lilly* is completely different than that of the present case. In *Lilly*, the claims were directed to novel insulin-encoding sequences which were not disclosed in (or

known prior to the filing of) the as-filed specification. In contrast, the pending claims are directed to biodetectors that are literally described in the specification and whose components were described in the specification and known in the art. Therefore, the findings in *Eli Lilly* have no bearing on the facts of the present application.

Federal Circuit decisions that are more germane to the case on appeal are *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 54 USPQ2d 1227 (Fed. Cir. 2000), *Capon v. Eshhar,* 76 USPQ2d 1078 (Fed. Cir. 2005), and *Falkner et al. v. Inglis et al.* (Fed. Cir. 2006, Docket No. 05-1324). Applicants note that *Union Oil, Capon* and *Falkner* are all more recent than *Eli Lilly* and *In re Gostelli.*

In *Union Oil v. Atlantic Richfield*, the Federal Circuit made clear that the specification need **not** describe the exact chemical composition of every claimed combination, adding that neither the Patent Act nor case law requires such detailed disclosure (*see, Union Oil* at 1233):

> Appellant refiners assert that the specification does not describe the exact chemical component of each combination that falls within the range claims of the '393 patent. However, neither the Patent Act nor the case law of this court requires such detailed disclosure. ...
>
> The inquiry for adequate written description simply does not depend on a particular claim format, but rather on whether the patent's description would show those of ordinary skill in the ... art that the inventors possessed the claimed invention at the time of filing.

In *Capon v. Esshar,* the Federal Circuit completely rejected the notion that the specification must describe information (*e.g.,* sequence data) that is either known or can readily be determined based on scientific facts (*Capon* at page 1085, emphasis added):

> The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. ...
>
> The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution.

The holding in *Capon* in particularly relevant to the instant case. In *Capon*, the Federal Circuit held that the precise sequence of a chimeric antibody need **not** be described because the components were well known. Likewise, in the instant case, the components of a chimeric transmembrane protein which initiates a cascade intracellularly are also well known.

In *Falkner,* the Federal Circuit reaffirmed that working examples are not required to satisfy the written description requirement, even for a broad genus (*see, Falkner,* page 14):

> Specifically, we hold, in accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.

With particular regard to recitation of known structures, the Federal Circuit cited *Capon* in reaffirming that adequate written description does not require re-description of the sequence of known molecules and that literature available at the time of filing must be considered in determining the adequacy of the written description (*Falkner*, pages 17-18):

> Indeed, a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement. It would neither enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention. As we stated in Capon, "[t]he 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution." Id. at 1358. Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (wherein permitted) of such genes and sequences.

The holding in *Falkner,* like the holdings in *Union Oil, Capon* (and the case law regarding written description generally), provides further support (if any is needed) that the

written description rejection in the case on appeal is unsustainable in view of the specification as a whole and the state of the art as exemplified by the literature of record. In light of these clear teachings of the Court, the Office's assertion, in the case on appeal, that Applicants are required to disclose multiple examples of particular biodetectors, is inconsistent with the requirements of the first paragraph of Section 112.[1]

Furthermore, as the Federal Circuit reiterated in *Capon* and *Falkner*, because each component of the claimed proteins was well known and described, the claimed subject matter is adequately described. Applicants have clearly evinced possession of the components of the claimed biodetectors and, accordingly, have satisfied the written description requirement.

Moreover, Applicants also amply describe that which is new, *i.e.,* biodetectors as claimed using known transmembrane protein cascades. Thus, clear description is present in the original claims and specification, and the written description requirement has therefore been satisfied. Applicants have shown possession of the claimed subject matter at the time of filing – clearly and unmistakably. As a result, the rejection cannot be sustained.

[1] Applicants also direct attention to Examples 9 and 14 of the PTO Guidelines on Written Description in which the Office clearly states that disclosure of a single representative species can adequately describe a broad genus. These Examples were favorably commented on by the Federal Circuit in *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002).

CONCLUSION

Applicants respectfully submit that the claims in condition for allowance.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Respectfully submitted,

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By: _____
Dahna Pasternak
Registration No. 41,411
Attorney for Applicants

ROBINS & PASTERNAK LLP
1731 Embarcadero Road, Suite 230
Palo Alto, CA 94303
Telephone (650) 493-3400
Facsimile (650) 493-3440